REMARKS/ARGUMENTS

Claims 15, 17, 20, 21, 26 to 29, 33, 35 and 38 have been amended for formal purposes and claims 16 and 22 have been cancelled. New claims 41 and 42 has been added and are based on claim 15. Neither the amendments to the claims, nor new claims 41 and 42 introduce new matter or raise new issues.

Claims 16 and 28 were rejected under 35 U.S.C. 112 second paragraph as indefinite. It is submitted this rejection is no longer proper and should be withdrawn.

Claim 16 has been cancelled thus rendering the rejection thereof moot. Claim 28 has been amended by deletion of the phrase "or of additional gastrointestinal complaints". Thus, claim 28 is no longer "unclear".

Claims 15 to 17, 21, 22, 27, 29 and 34 were rejected under 35 U.S.C. 102(b) as anticipated by the Product Alert Bulletin (PROMT Abstract). It is submitted this rejection is improper and should be withdrawn.

For a prior art reference to anticipate a claimed invention, that reference must show each and every feature of that invention and must show those features arranged as in the claimed invention. See *Connell v. Sears, Roebuck & Co.*, 220 U.S.P.Q. 193 (Fed. Cir. 1983). Further, the reference must contain an enabling disclosure so that one of ordinary skill in the art can make and practice the invention without undue experimentation. It is submitted that the reference does not anticipate the claimed subject matter and the rejection for anticipation is in error as a matter of law. Further, the Examiner is again requested to make of record the entirety of the article rather than just the Abstract.

Claim 15, as amended, does not recite a combination of the *Tanacetum parthenium* and ginger as a member of the Markush group but does recite the combination of *Tanacetum parthenium* with at least one of *Vitex agnus-castus* and/or *Cimicifuga racemosa*. Thus, the reference does not identify the now claimed invention.

Further, the reference does not enable one of ordinary skill in the art to make an herbal pharmaceutical preparation. It is clear that the abstract is referring to a food product. Apparently, the Examiner inferred from the name of the product, Migra-Wonder™, which apparently is used as a trade name for the product, that it has the ability to treat migraine headaches. The Examiner's inference is pure speculation and nothing in the abstract suggests that which the Examiner assumes. If Alvita Teas is claiming trademark status to Migra-Wonder™, that mark cannot be descriptive of

the product or any of its properties. Thus the reference fails to identify and fails to enable the invention of each of the pending claims.

Accordingly, the rejection under 102(b) is improper as a matter of law and should be withdrawn.

Claims 15 to 17, 21 to 23, 26 to 30, 33 and 34 were rejected under 35 U.S.C. 103(a) as unpatentable over WO 96/22774 ("WO '774"), the PROMT Abstract (July 1996), Journal of Natural Products, 1992 (Marles) and the admitted state of the art.

WO '774 discloses a preparation containing certain lactones, such as parthenolide, and Vitamin B complexes, such as riboflavin, for the treatment of migraines, cluster headaches, arthritis and bronchial complaints. It is the basic combination of parthenolide and B-complex vitamins which the reference mentions as leading to "synergistic effects". See WO '774, page 3, lines 12 to 15. Further, the ranges disclosed by the reference for the amount of feverfew are those based on the synergistic effect resulting from the required Vitamin B. Clearly, when low amounts of Vitamin B are present the amount of feverfew is substantially increased and exceeds the amounts set forth for instance in claims 23 and 35. The amounts recommended clearly exceed those recited. See Examples 1 to 5.

The Examiner apparently is referring to pages 1 to 6 of the reference and in particular the listing of additional ingredients starting on page 5 and continuing on to page 6. The introductory phrase to that listing is that the combination of feverfew and Vitamin B may optionally include other known anti-migraine preparations, sedatives and relaxants, analgesics and anti-emetics. Following this introductory phrase, there is a listing of 34 additional ingredients. The reference never discloses which of those ingredients in combination with the lactone and Vitamin B ingredients are useful for any of the generally referred to conditions. Further, there are no amounts specified for any of the additional ingredients. For instance, ginger has been previously known to be useful as a relaxant in tea. Thus, assuming one of ordinary skill in the art chose ginger as the third component (although it is not clear from this reference why one would make that choice), the skilled art worker would still not know the relative amounts.

Starting on page 7, WO '774 lists another 38 additional additives including analgesics and NSAIDS. As such, WO '774 does not identify the claimed invention nor does it contain disclosure to enable one of ordinary skill in the art to practice the invention. Thus, WO '774 cannot, as a matter of law, render the now claimed subject matter obvious.

The reference does not suggest a synergistic effect resulting from combining any of the substances listed on pages 5 to 7 with feverfew.

The deficiencies of the PROMT Abstract have been discussed above and those comments should be considered as if set forth here at length.

Marles proposes a bioassay to be used, presents an analysis of various sources of parthenium, and discusses the limits of the proposed assay. Marles main point is the new bioanalytical technique. The reference does not go beyond the previously cited prior art or that which has been discussed in the specification.

On page 1050 of the 1992 article, Marles discusses the theory underlying the bioassay. In particular, there is a discussion of the role that seratonin is believed to play in the pathogenesis of migraine headaches. However, Marles admits that the precise role of platelets and 5-HT are quite controversial. However, today seratonin release or update models are more commonly used in connection with depression models.

Marles is at best cumulative, adds nothing to the rejection and certainly does not suggest the now claimed subject matter.

It is submitted that the Examiner's conclusion of obviousness based on the above-discussed art is erroneous. The record relied upon by the Examiner contains no more than generalized statements which could mean a number of different things in different contexts and could apply to a number of different conditions. Thus, there is not a proper basis for a conclusion of obviousness based on the combination of references and it is submitted that a prima facie case of obviousness has not been made out.

Further, there is no motivation for the combination of references. It is submitted the Examiner has improperly combined the references. The Examiner's states that the idea for combining the references "flows logically" from their having been used individually in the prior art. However, each of the cases that the Examiner cites in support of that proposition predate the creation of the Federal Circuit and its decisions specifically requiring that the prior art must provide motivation for the combination. It is submitted that the standard relied on by the Examiner with respect to the combination is in direct contradiction to the current standard. The references cited do not suggest the combination now defined in the claims. See *In re Grabiak* 226 U.S.P.Q. 870 (Fed. Cir. 1985).

Claims 15 to 40 were rejected under 35 U.S.C. 103(a) as unpatentable over the June 1998 PROMT Abstract ("Wyandt"), Castleman (The Healing Herbs), Marles and PDR for Herbal Medicine, POPP and the admitted state of the art in view of U.S. Patent No. 5,443,850 to Thys-Jacobs. It is submitted this rejection is improper and should be withdrawn.

Wyandt is nothing more than a collection of comments regarding known herbal substances. In almost every case, Wyandt indicates there is little or no scientific evidence to support the asserted benefits of each of the substances. The reference separately mentions feverfew and ginger. However, the reference makes no suggestion and provides no motivation to combine for any purpose any of the 12 or more herbs mentioned in Wyandt. Further, the reference makes no mention of any of the other components recited in, for instance, claim 15.

The Wyandt PROMT citation does no more than repeat vague generalities about parthenium and ginger. It thus appears that this reference is duplicative of other cited references or material of record.

Marles has been discussed above and those comments should be considered as if set forth here at length.

Castleman appears to be a collection of the history and folklore regarding ginger. However, Castleman adds nothing to the above discussed references vis-à-vis the claimed invention. There is no mention in Castleman of any controlled studies showing the efficacy or safety of the substance. Castleman's only reference to a possible study is that published in Lancett where less than 1 g was used to prevent nausea from motion sickness and the statement that Chinese physicians recommend 20 to 28 gms. to trigger menstruation. The Examiner's citation of Castleman makes no mention of other components recited in claim 15. Castleman alone, or in combination, does not render the claimed subject matter obvious.

The PDR for Herbal Medicines does not support the rejection for obviousness. To the contrary, it notes that the prior believed effects of the herb *Cimicifuga* are not supported by research results. The "indications and usage" heading generally refers to climacteric complaints or ailments and there is no mention of treatment of migraines.

POPP does no more than mention *Vitex agnus castus* as useful for treating numerous syndromes including PMS (which is different than migraine or menstrual cramps). The Examiner is requested to make the article, or the referred to European patent, of record if it is not already of

record. However, this reference in and of itself is not enabling and adds nothing to the rejection for obviousness.

Further, there is no prior art admissions on pages 5 and 6 of the present specification regarding use of *Vitex agnus-castus* or *Cimicifuga racemosa* for treatment of migraines.

U.S. Patent 5,443,850 is cited only for its review of statistical information in column 1 at about lines 22 to 49. However, the reference discloses a totally different approach and utilizes combinations of calcium and Vitamin D to treat the condition. The reference makes no mention of herbal treatments, indicates that a significant percentage of migraine sufferers include men and names such substances as NSAIDS (aspirin and naproxen) as therapeutic agents used in treatment. Thus, this reference is either non-analogous art or teaches away from the now claimed invention.

It is submitted that the conclusion of obviousness based on the cited references is improper and should be withdrawn. The number of references which the Examiner has combined illustrates the unobviousness of the now claimed subject matter and strongly suggests that the rejection is the product of hindsight reconstruction using Applicants' disclosure as a template.

It is submitted that the rejection improperly combines the prior art references and does so through the lens of hindsight reconstruction. The references taken alone, or in combination, do no more than establish that the individual components were known in the art. However, this does not by itself provide motivation for the combination, see In re *Grabiak*, supra. As discussed above, the cases cited on page 7 of the Official Action do not employ the proper standard for combining references. It is therefore submitted the Examiner has not established a prima facie case.

Further, none of the references, alone or in combination, anticipate or render claims 41 or 42 obvious.

With respect to the Examiner's discussion starting on page 8 of the Official Action, concerning previously submitted arguments, Applicant has again requested that the entirety of the Product Alert Bulletin be made of record. Applicant does not agree that the article is the "full-text" enabled article. It apparently is an abstract from an advertisement or product brochure. It is not enabling.

The Examiner states that WO '774 clearly discloses to the skilled artisan that the bioactive lactone can beneficially be combined with ginger for therapeutic effects. Applicant sees no such disclosure. To the contrary, WO '774 discloses that it is the combination of the lactone with the Vitamin B constituent which provides the therapeutic effects. There is no specific therapeutic effect

attributed to any of the additional 34 ingredients in the first list. The compounds in the second list starting on page 7 of WO '774 are all pharmaceutically known compounds each with specific activities. That list includes analgesic compounds such as aspirin, ibuprofen, naproxen, phenylbutazone, diclofenac to name just a few. With the inclusion of extensive lists of analgesics, such as set forth on pages 7 and 8 of WO '774, the Examiner's conclusion that the reference teaches beneficial therapeutic affects for the lactone combined with ginger is simply not supported. No example of this reference combines feverfew with ginger or any ingredient recited in claim 15. However, as pointed out above, the claimed invention requires the presence of at least one of *Vitus agnus-castus* and *Cimicifuga racemosa*.

Further, the combination of references proposed by the Examiner and his interpretation of WO '774 requires that a significant component of the reference composition be disregarded, i.e. the Vitamin B complex component. This is improper See *In re Ratti*, 123 U.S.P.Q. 349 (CCPA, 1959).

The Examiner states that Applicants have discussed the various cited references individually without addressing the combined teachings. With all due respect, the Examiner has cited the references individually and only given generalized conclusions of the results of the combined references. This does not constitute a prima facie case. As indicated above, Applicant believes the combination of references is improper and the manner in which they have been combined requires that significant parts of at least one of the references must be ignored. This is improper under 35 U.S.C. 103.

Submitted herewith is the declaration of the inventor Stefan Spiess. This declaration reports on tests which were conducted to show the unexpected beneficial results that come about through the practice of the invention.

The Spiess declaration discusses a model for testing for migraine treatment, the testing protocol as well as two in-vitro tests based on cells of rat microglia, one for Prostaglandin E_2 (PGE_2) the other for Nitric Oxide (NO). PGE_2 and NO were measured as markers for inflammation and pain. Inhibition of PGE_2 and Nitric Oxide (NO) release results in reduction of inflammation and pain. The results in summary show:

1) Test for *Tanacetum*: strongly and dose dependent inhibition of NO and PGE_2 release;
2) Test for *Cimicifuga*: slightly and dose dependent inhibition of NO release; PGE_2, release is reduced;

3) Test for *Vitex agnus-castus*: NO not affected; PGE_2 level is back to control level for high doses;

4) Test for a combination of *Tanacetum* and *Cimicifuga*: NO release is potently prevented compared with *Tanacetum* alone; PGE_2 release is synergistically prevented compared to *Tanacetum* alone;

5) Test for a combination of *Tanacetum* and *Vitex agnus-castus*: PGE_2 release synergistically prevented compared to *Tanacetum* alone; and

6) Test for a combination of *Tanacetum*, *Cimicifuga* and *Vitex agnus-castus*: NO release is more potently prevented than with *Tanacetum* alone; PGE_2 release is potently inhibited in the 3 component combination.

The studies thus establish a synergistic inhibiting effect of the combination of *Tanacetum parthenium* with one of, and both of, *Vitex agnus-castus* and *Cimicifuga racemosa*. The above conclusions are supported based on the figures attached to the Spiess declaration.

In view of the foregoing, reconsideration and allowance of the application with claims 15, 17 to 21 and 23 to 42 are earnestly solicited.

The Examiner is invited to phone applicant's undersigned attorney to advise of the status of the application after of reviewing the foregoing so as to minimize any needless expense or delay.

It is believed that no fees or charges are required at this time in connection with the present application; however, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
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